CLAIMS

What is claimed is:

1. A method for determining whether a subject has neoplasia, comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression, wherein detection of Mdm2 expression elevated above normal and HAUSP expression elevated above normal in the diagnostic sample is diagnostic of neoplasia in the subject.

2. The method of claim 1, wherein the neoplasia is a carcinoma, a lymphocytic leukemia, a myeloid leukemia, a malignant lymphoma, a malignant melanoma, a myeloproliferative disease, a sarcoma, or a mixed type of neoplasia.

3. The method of claim 1, wherein the neoplasia is an Mdm2- or HAUSP-associated neoplasia.

4. The method of claim 1, wherein the neoplasia is a p53-associated neoplasia.

5. The method of claim 1, wherein Mdm2 expression elevated above normal and HAUSP expression elevated above normal are detected in the diagnostic sample by detecting Mdm2-HAUSP interaction elevated above normal in the diagnostic sample.

6. The method of claim 1, wherein the diagnostic sample is assayed using an agent reactive with Mdm2 and an agent reactive with HAUSP.

7. The method of claim 6, wherein at least one agent is labeled with a detectable marker.

8. The method of claim 6, wherein at least one agent is an antibody.

9. The method of claim 1, wherein the diagnostic sample is assayed using a nucleic acid probe which hybridizes to nucleic acid encoding Mdm2 and a nucleic acid probe which hybridizes to nucleic acid encoding HAUSP.

10. The method of claim 9, wherein each nucleic acid probe is DNA or RNA.

11. The method of claim 10, wherein at least one nucleic acid probe is labeled with a detectable marker.

12. A method for assessing the efficacy of therapy to treat neoplasia in a subject who has undergone or is undergoing treatment for neoplasia, comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression, wherein detection of normal Mdm2 expression and normal HAUSP expression in the diagnostic sample is indicative of successful therapy to treat neoplasia, and detection of Mdm2 expression elevated above normal and HAUSP expression elevated above normal in the diagnostic sample is indicative of a need to continue therapy to treat neoplasia.

13. The method of claim 12, wherein Mdm2 expression elevated above normal and HAUSP expression elevated above normal are detected in the diagnostic sample by detecting Mdm2-HAUSP interaction elevated above normal in the diagnostic sample.

14. A method for assessing the prognosis of a subject who has neoplasia, comprising assaying a diagnostic sample of the subject for Mdm2 expression and HAUSP expression, wherein the subject's prognosis improves with detection of a decrease in Mdm2 expression and a decrease in HAUSP expression in the diagnostic sample, and the subject's prognosis worsens with detection of an increase in Mdm2 expression and an increase in HAUSP expression in the diagnostic sample.

15. The method of claim 14, wherein Mdm2 expression and HAUSP expression are detected in the diagnostic sample by detecting Mdm2-HAUSP interaction in the diagnostic sample.

16. A kit for use in detecting neoplasia, comprising:

(a) at least one agent reactive with Mdm2;

(b) at least one agent reactive with HAUSP; and

(c) reagents suitable for detecting expression of Mdm2 and expression of HAUSP.

17. The kit of claim 16, wherein at least one agent is labeled with a detectable marker.

18. A method for treating neoplasia in a subject, comprising increasing activity of p53 in the subject, wherein activity of p53 is increased in the subject by modulating Mdm2-HAUSP interaction in the subject.

19. The method of claim 18, wherein the neoplasia is a carcinoma, a lymphocytic leukemia, a myeloid leukemia, a malignant lymphoma, a malignant melanoma, a myeloproliferative disease, a sarcoma, or a mixed type of neoplasia.

20. The method of claim 18, wherein the neoplasia is an Mdm2- or HAUSP-associated neoplasia.

21. The method of claim 18, wherein the neoplasia is a p53-associated neoplasia.

22. The method of claim 18, wherein Mdm2-HAUSP interaction is modulated in the subject by administering a modulator of Mdm2-HAUSP interaction to the subject.

23. The method of claim 22, wherein the modulator is administered to the subject orally, intradermally, intramuscularly, intraperitoneally, intravenously, or subcutaneously.

24. A method for deubiquitinating and/or stabilizing Mdm2 in a cell, comprising contacting the cell with HAUSP, in an amount effective to deubiquitinate and/or stabilize Mdm2.

25. The method of claim 24, wherein the contacting is effected *in vitro*.

26. The method of claim 24, wherein the contacting is effected *in vivo* in a subject.

27. The method of claim 26, wherein the contacting is effected *in vivo* in a subject by administering HAUSP to the subject.

28. The method of claim 27, wherein HAUSP is administered to the subject orally, intradermally, intramuscularly, intraperitoneally, intravenously, or subcutaneously.

29. The method of claim 26, wherein the subject is a human.

30. The method of claim 29, wherein the human has neoplasia.

31. The method of claim 30, wherein the neoplasia is a carcinoma, a lymphocytic leukemia, a myeloid leukemia, a malignant lymphoma, a malignant melanoma, a myeloproliferative disease, a sarcoma, or a mixed type of neoplasia.

32. The method of claim 30, wherein the neoplasia is an Mdm2- or HAUSP-associated neoplasia.

33. The method of claim 30, wherein the neoplasia is a p53-associated neoplasia.

34. The method of claim 30, wherein the HAUSP treats the neoplasia in the subject.

35. A method for modulating deubiquitination and/or stability of p53 in a cell, comprising contacting the cell with a modulator of Mdm2-HAUSP interaction, in an amount effective to modulate deubiquitination and/or stability of p53.

36. The method of claim 35, wherein deubiquitination of p53 is increased, and stability of p53 is increased, in the cell.

37. The method of claim 36, wherein p21 is induced in the cell by p53.

38. The method of claim 35, wherein the contacting is effected *in vitro*.

39. The method of claim 35, wherein the contacting is effected *in vivo* in a subject.

40. The method of claim 39, wherein the contacting is effected *in vivo* in a subject by administering the modulator to the subject.

41. The method of claim 39, wherein the subject is a human.

42. The method of claim 41, wherein the human has neoplasia.

43. The method of claim 42, wherein the neoplasia is a carcinoma, a lymphocytic leukemia, a myeloid leukemia, a malignant lymphoma, a malignant melanoma, a myeloproliferative disease, a sarcoma, or a mixed type of neoplasia.

44. The method of claim 42, wherein the neoplasia is an Mdm2- or HAUSP-associated neoplasia.

45. The method of claim 42, wherein the neoplasia is a p53-associated neoplasia.

46. The method of claim 42, wherein the modulator of Mdm2-HAUSP interaction treats the neoplasia in the subject.

47. A method for identifying a modulator of Mdm2-HAUSP interaction, comprising the steps of:

(a) obtaining or generating an *in vitro* system comprising Mdm2 and HAUSP;

(b) contacting the *in vitro* system with a candidate modulator; and

(c) determining if the candidate modulator modulates Mdm2-HAUSP interaction in the *in vitro* system.

48. The method of claim 47, wherein the determination in step (c) is made by comparing Mdm2-HAUSP interaction in the *in vitro* system of step (b) with Mdm2-HAUSP

interaction in a second *in vitro* system comprising Mdm2 and HAUSP in the absence of the candidate modulator.

49. The method of claim 47, wherein the determination in step (c) is made by comparing Mdm2-HAUSP interaction in the *in vitro* system of step (b) with Mdm2-HAUSP interaction in a second *in vitro* system comprising Mdm2, HAUSP, the candidate modulator, and an anti-Mdm2 or anti-HAUSP antibody or antagonist.

50. A modulator identified by the method of claim 47.

51. A method for treating an Mdm2-, HAUSP-, or p53-associated condition in a subject, comprising administering to the subject an amount of the modulator of claim 50 effective to treat the Mdm2-, HAUSP-, or p53-associated condition in the subject.

52. Use of a modulator of Mdm2-HAUSP interaction in a method of treating neoplasia.

53. A pharmaceutical composition, comprising an effective amount of a modulator of Mdm2-HAUSP interaction, and a pharmaceutically-acceptable carrier.

54. A method for identifying an agent that is reactive with Mdm2, comprising the steps of:

(a) contacting a candidate agent with Mdm2, in the presence of HAUSP; and

(b) assessing the ability of the candidate agent to inhibit Mdm2-HAUSP interaction.

55. The method of claim 54, further comprising the steps of:

(c) contacting the candidate agent with one or more cells comprising Mdm2, HAUSP, or p53; and

(d) determining if the agent has an effect on one or more Mdm2-, HAUSP-, or p53-associated biological events in the one or more cells.

56. An agent identified by the method of claim 54.

57. A method for identifying an agent that is reactive with HAUSP, comprising the steps of:

(a) contacting a candidate agent with HAUSP, in the presence of Mdm2; and

(b) assessing the ability of the candidate agent to inhibit HAUSP-Mdm2 interaction.

58. The method of claim 57, further comprising the steps of:

(c) contacting the candidate agent with one or more cells comprising Mdm2, HAUSP, or p53; and

(d) determining if the agent has an effect on one or more Mdm2-, HAUSP-, or p53-associated biological events in the one or more cells.

59. An agent identified by the method of claim 57.

60. A complex comprising Mdm2 and HAUSP.